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Two-dimensional nanopores and nanoporous membranes for ion and molecule transport

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Two-dimensional (2D) materials from graphene to metal dichalcogenides and beyond, have interesting electrical, optical and mechanical properties. Recent advances in their growth, transfer and device physics have led to the shrinking of 2D material-based devices to the atomic scale and expanding their functionality. Single or multiple nanometer-scale holes, as small as single-atom vacancies, can be introduced in suspended atomically-thin 2D membranes, giving rise to nanopore and nanoporous devices, respectively. While engineering vacancies and holes is interesting for modulating optoelectronic properties, one equally fascinating research focus is ion and molecule transport through such pores in thin membranes. Here, we review the advancement of 2D nanopore science and technology for biomolecular detection and analysis, including DNA sequencing, and the largely parallel efforts towards development of 2D nanoporous membranes for ion selectivity and water desalination, both directions sharing similar fundamental principles.

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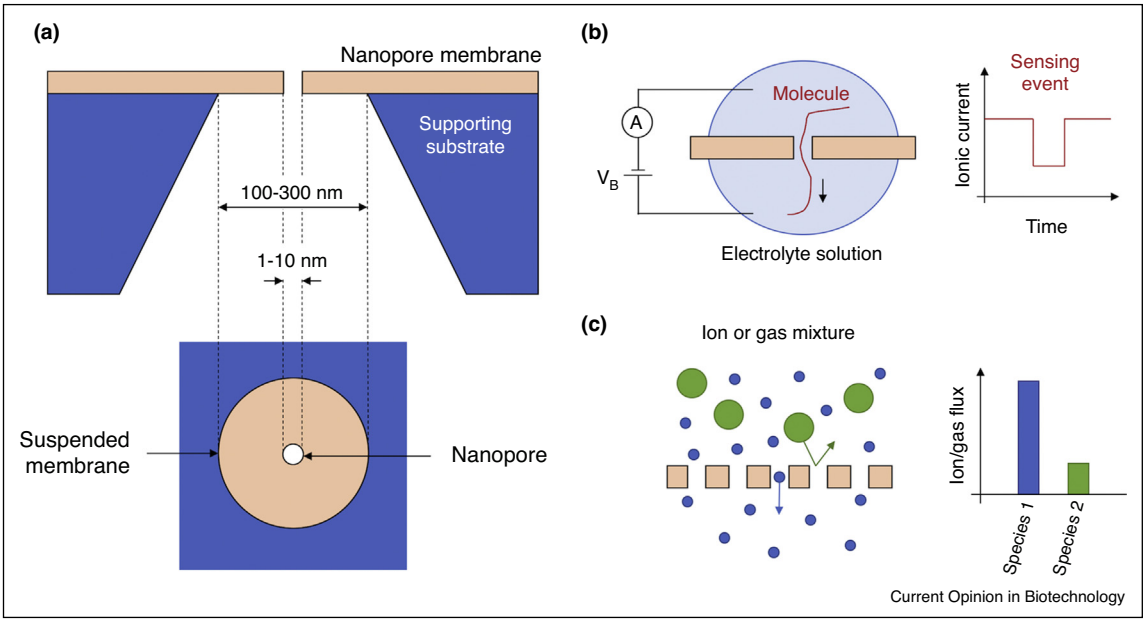
Atomically-thin two-dimensional (2D) materials have been studied since 1940s [1], but the first isolation of such a nanomaterial—graphene—was demonstrated in 2004 [2]. This discovery led to further isolation of other 2D materials (transition metal dichalcogenides or TMDs, hexagonal boron nitride or h-BN, phosphorene, etc.). Their low dimensionality results in improved electrical, mechanical and chemical properties over bulk. The ionic and gas impermeability of 2D sheets can be exploited to make transmembrane devices with nanoscale pores allowing only molecules of specific sizes and charges to pass through. Atomically-thin 2D materials provide advantages over thicker 3D membranes such as stronger signals for molecular detection and larger flux for filtration purposes [3•,4•]. Here we review 2D membranes for molecular sensing for biomedical applications and ion selectivity for water desalination applications. 2D membranes have also been recently investigated for selective gas flow [5,6].

2D nanopore sensors

Nanopore sensors are nano-Coulter counters [7] (Figure 1a). When the sensor is immersed in an electrolyte solution and voltage is applied, ions flow through the pore. If a particle is driven through the pore, the ionic concentration inside the pore decreases [8] (or increases) [9,10], resulting in a change in the ionic current (Figure 1b), the magnitude and duration of which depend on the dimensions and charge density of the particle and the pore. One of the most popular applications for nanopores is DNA sequencing [3•]. Solid-state nanopores may be able to sequence single-stranded DNA by discriminating nucleotides due to their size differences resulting in different levels of current blockage [11,12]. Protein nanopores like α-hemolysin [13] and MspA [14] have been shown to sequence DNA and progress has been achieved in transitioning research into application [15]. Solid-state nanopore literature mostly relies on silicon nitride [16], silicon oxide [17] and amorphous silicon pores [18] and techniques common in the industry were adapted for their fabrication [9,17,19,20].

While solid-state nanopores may be ultimately robust to chemical and mechanical conditions, there are existing limitations. To increase the ionic signal, one can start with 2D membranes, or with thicker three-dimensional membranes that are thinned [9,11,18,20,21]. Si-based pores form stable nanopores to about 1-nm-thickness [18,22] and can be stable down to 0.7 nm, making them competitive with 2D nanopores [18,22]. The membrane stoichiometry can be modified to tune the Si to N ratio. Laser etching of SiN_x membranes was also reported to produce thin nanopores [23•,24•,25,26]. Two-dimensional nanopores based on graphene, h-BN and TMDs have been demonstrated to detect DNA translocations (Figure 2a–d) [8,27–33]. Atomically-thin membranes were transferred [34] across holes on SiN_x membranes, and grown directly across holes [35,36]. 2D membranes have been transferred also on glass chips [37–40] and capillaries [41,42]. Such insulating substrates reduce capacitance

Figure 1



Schematic of typical nanopore sensor chips and nanoporous membranes. **(a)** Cross-sectional and top view of a silicon-based or 2D material membrane ('nanopore membrane') with a nanopore suspended over a circular aperture in a supporting substrate (e.g. silicon, glass). **(b)** Voltage-induced translocation of an elongated charged molecule (like DNA) through a single nanopore immersed in an electrolyte solution (left) giving rise to ionic current changes, representing a sensing event (right). **(c)** Size-dependent molecule species (ion or gas) rejection through a membrane with multiple nanopores or a nanoporous membrane (left) resulting in a variable molecule flux (right).

and noise. Noise can also be lowered by decreasing the electrolyte contact area [43].

MoS_2 nanopores have been reported to differentiate between isolated individual nucleotides using ionic liquids [12]. An important transformative advantage of 2D nanopores is their signal-to-noise ratio and spatial resolution. Thin nanopores lead to large ionic currents due to decreased nanopore resistance, and only a small section of the molecule resides in the pore at any given time. Molecular dynamics studies of graphene nanopores have found that in three-layer graphene pores, hydrophobic interactions lead to reduction in the conformational fluctuations of the nucleotides [44]. Most of the new 2D materials are hydrophobic and nanopore wetting was ensured by first immersing the nanopores in ethanol/water [32,33]. MoS_2 nanopores have also been used for power generation [45], and non-linear ion-current versus voltage curves have been measured in sub-nm diameter MoS_2 nanopores, [43,46] in contrast to linear current–voltage curves [32,33]. WS_2 nanopores readily allow DNA translocation with similar noise levels to MoS_2 [33]. The atomic configuration at the pore edge affects the ion concentration profile [47•], as observed for MoS_2 pores where the classical equation of pore conductance fails to describe the conduction in sub-1-nm diameter pores [47•,48•]. Recently, data from triangularly-shaped pore in BN were compared to circularly-shaped MoS_2 pores [49]. Hydrophilic 2D pores in phosphorene were also made [50,51]. 2D materials further possess opportunities for band-gap engineering. Emerging 2D materials, like 2D MXenes [52], can further enrich the 2D nanopore research.

Other geometries including 2D nanoribbons (NR) and nanoelectrodes are also being explored. In the case of 2D nanoribbons with nanopores, the sensing is via the out-of-plane ionic signal and the in-plane electronic signal in the nanoribbon. Recent studies [53–55] calculated NR signals from nucleic acids for different NR widths, edge structure and pore position. Qiu *et al.* further modeled graphene and MoS_2 NRs [56]. An analysis of expected signals and noise for experimentally realistic conditions was also reported [57•]. Because the nanoribbon-nanopore device turns voltage changes into current changes in the ribbon channel, transconductance, that is, the ribbon current gained by changing the gate voltage, is an important experimental parameter to be maximized.

At high frequencies, high-transconductance nanoribbon-nanopore devices can outperform ionic current measurements [57•]. Realizations of these ideas include Si wires [58] and graphene nanoribbons [59–61]. Here, experimental efforts include minimization of defects in the 2D material [61], and encapsulation [59,60,62], to prevent leakage currents. Similar efforts include carbon